1106

TREATMENT WITH FK 506 OF STEROID RESISTENT FOCAL SCLEROSING GLOMERULONEPHRITIS (FSGN) OF CHILDHOOD

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Focal sclerosing glomerulonephritis (FSGN) is the leading cause of steroid resistant nephrotic syndrome in childhood. Cytotoxic agents may induce remission but jeopardize future fertility. Cyclosporin (CyA) has reduced proteinuria at the cost of progressive renal failure, probably contributed to by drug nephrotoxicity (1-2). We have used FK 506 to treat FSGN. A previously healthy 19 month old boy developed periorbital and peripheral edema November 1988. Urinalysis revealed 4+ protein but was otherwise unremarkable. Other laboratory data included: creatinine 0.77 mg/dl, BUN 16 mg%, albumin 1.8 gm% and serum cholesterol 411 mg%. Antinuclear antibodies, C3, C4, hepatitis B screen, and antistreptolysin-O (ASLO) titers were normal. Prednisone (175 mg/day) was started but the proteinuria was not reduced during 7 months of therapy and the steroids were tapered to 35 mg/day. Increasing peripheral edema and ascites necessitated two hospital admissions for intravenous diuretic therapy. A renal biopsy after 9 months showed focal and segmental glommerulosclerosis with moderate interstitial fibrosis. A course of cyclophosphamide did not alter the proteinuria.

At 30 months of age he was referred to us with grossly cushingoid features and anasarca. He was receiving high dose loop diuretics and metolazone. Oral FK 506 (0.15 mg/kg/bid) was started and prednisone was reduced to 5 mg/day, and after 4 weeks, stopped. There was dramatic and progressive improvement clinically, and in the laboratory findings (Table 1). Diuretics

were discontinued. He was experienced no side effects of FK 506 to date, now after 15 of weeks of therapy.

A complete remission of FSGN occurred in this patient without a reduction in renal function, something not accomplished in previous reports of CyA induced remission of FSGN and other forms of steroid resistent nephrotic syndrome (1-4). We have recently reported that FK 506 in liver transplant recipients is more potent and less nephrotoxic than CyA (5). Our observations in this child as well as our recent successful treatment of CyA induced hemolytic uremic syndrome (6) suggests that FK 506 may be effective in a wide variety of renal and extra-renal immune mediated disorders. Cautious attempts will be in order to reduce the FK 506. There is no reason to assume that the present dose will be required for maintenance.

The immediate response of a 41 year old male has been similar to that of the child, although it is too early to say more. The second patient with mesangial proliferative glomerulonephritis and steroid resistent nephrosis of 6 months duration (6-10 grams/day urine protein) was treated with 0.15 mg/kg FK 506 starting on 13 February 1990 and with the discontinuance of 100 mg/day prednisone. Within the next 10 days, urinary protein declined to 1485 mg, serum cholesterol fell from 360 to 240 mg/dl, and creatinine clearance remained the same.

TABLE 1

	CREATININE MG/DL	BUN MG/DL	CREAT.CL ML/1.73M^2	URINE PROTEIN MG/24 h	CHOLESTEROL MG/DL	SERUM ALBUMIN GM/DL
11/88	0.7	16	77.5	4+	411	1.8
5/89	0.4	6				1.6
9/89	0.3	15			630	1.7
11/19/89	0.3	6	82.0	1,406		
11/20/89			FK 506 STARTED			
11/27/89	0.1	10		154		
12/15/89	0.4			147		
1/12/90	0.2	13	87.9	25	142	2.9
3/1/90	0.1	9	86	63	169	3.7

SI Conversion --- Creatinine - mmol/l = mg/dl x 88.4
BUN - mmol/l = mg/dl - 6
Cholesterol - mmol/l = mg/dl - 38.7
Albumin - gm/dl x 100

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